PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
P032364WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB 03/06281	17/11/2003	15/11/2002
Applicant		
CHIRON SRL		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[X] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[X] furnished subsequently to this Authority in computer readble form.

[X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

UNEXPECTED SURFACE PROTEINS IN NEISSERIA MENINGITIDIS

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

[X] as suggested by the applicant.

[ ] None of the figures.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

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national application No.
PCT/IB 03/06281

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-5 (all partly)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Inventions 1-158: claims 1-5 (all partly)

Inventions 1-158:
A compostion comprising (a) outer-membrane vesicles (OMV's) prepared from a first strain of Neisseria meningitidis and (b) one or more proteins which are present in OMV's prepared froma second strain of Neisseria meningitidis, but which are not present in OMV's prepared from said first strain. Furthermore the specification of (b), the use of OMV's of genetically-modified strains of Neisseria meningitidis comprising proteins not present in OMV's prior to modification and furthermore the specification of the protein of (b) as set out in claims 4 or 5.
Each of the inventions 1-158 specifically and respectively relates to one of the proteins set out in claims 4 or 5 e.g. for invention 1, NMB0007 etc... to invention 158, NMB2159.

Inventions 159-375: claims 6-8 (all partly)

Inventions 159-375:
A lipid bilayer including each and respectively a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO's: 1-217 or diverse variants, fragments or hybrids thereof. Furthermore the specification of the lipid bilayer and the said lipid bilayer which does not include some native membrane components.
Each of the inventions 159-217 specifically and respectively relates to one of the proteins set out in SEQ ID NO's 1-217 e.g. for invention 159, SEQ ID NO: 1 etc... to invention 375, SEQ ID NO: 217.

Inventions 376-592: claims 10-13 (all partly)

Inventions 376-592:
A protein comprising each and respectively an amino acid sequence selected from the group consisting of SEQ ID NO's: 1-217 or diverse variants, fragments or hybrids thereof. Furthermore a nucleic acid encoding each of said proteins.
Each of the inventions 376-592 specifically and respectively relates to one of the proteins set out in SEQ ID NO's 376-593 e.g. for invention 376, SEQ ID NO: 1 etc... to invention 593, SEQ ID NO: 217.

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[redacted]nal Application No
PCT/IB 03/06281

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/095 C07K14/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, MEDLINE, WPI Data, PAJ, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CLAASSEN I ET AL: "Production, characterization and control of a Neisseria meningitidis hexavalent class 1 outer membrane protein containing vesicle vaccine" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 14, no. 10, 1 July 1996 (1996-07-01), pages 1001-1008, XP004057632 ISSN: 0264-410X page 1002, left-hand column	1-3
Y	same citations -/--	4

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 June 2004	16. 11. 2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Steffen, P

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Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	-& VAN DER LEY P ET AL: "Construction of Neisseria meningitidis strains carrying multiple chromosomal copies of the porA gene for use in the production of a multivalent outer membrane vesicle vaccine" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 13, no. 4, 1995, pages 401-407, XP004057740 ISSN: 0264-410X page 404, right-hand column, paragraph 2 - page 405, right-hand column, paragraph 1	
X	WO 01/52885 A (PIZZA MARIAGRAZIA ;RAPPUOLI RINO (IT); CHIRON SPA (IT); GIULIANI M) 26 July 2001 (2001-07-26) page 2 - page 10 page 50 - page 52	1-3
X	WO 00/25811 A (GORRINGE ANDREW RICHARD ;HUDSON MICHAEL JOHN (GB); MICROBIOLOGICAL) 11 May 2000 (2000-05-11) page 2 - page 6	1,2
Y	NORAIS NATHALIE ET AL: "Combined automated PCR cloning, in vitro transcription/translation and two-dimensional electrophoresis for bacterial proteome analysis" PROTEOMICS, vol. 1, no. 11, November 2001 (2001-11), pages 1378-1389, XP009032238 ISSN: 1615-9853 page 1382, left-hand column, paragraph 1 - page 1383, left-hand column, paragraph 1; table 2	4
Y	DATABASE UNIPROT 'Online! EBI; 1 October 2000 (2000-10-01), TETTELIN ET AL.: "Cell division ATP binding protein FtsE" XP002284894 Database accession no. Q9K1R3 the whole document	4

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GRIFANTINI R ET AL: "Previously unrecognized vaccine candidates against group B meningococcus identified by DNA microarrays" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 20, no. 9, September 2002 (2002-09), pages 914-921, XP002272872 ISSN: 1087-0156 page 917, right-hand column, paragraph 2 - page 918, left-hand column, paragraph 1; figure 2; tables 2,3	
A	PIZZA M ET AL: "IDENTIFICATION OF VACCINE CANDIDATES AGAINST SEROGROUP B MENINGOCOCCUS BY WHOLE-GENOME SEQUENCING" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 287, no. 5459, 10 March 2000 (2000-03-10), pages 1816-1820, XP000986271 ISSN: 0036-8075 page 1817 - page 1818; table 1	
A	TETTELIN H ET AL: "COMPLETE GENOME SEQUENCE OF NEISSERIA MENINGITIDIS SEROGROUP B STRAIN MC58" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 287, 2000, pages 1809-1815, XP000914963 ISSN: 0036-8075 the whole document	
A	JOLLEY KEITH A ET AL: "Immunization with recombinant Opc outer membrane protein from Neisseria meningitidis: Influence of sequence variation and levels of expression on the bactericidal immune response against meningococci" INFECTION AND IMMUNITY, vol. 69, no. 6, June 2001 (2001-06), pages 3809-3916, XP002284891 ISSN: 0019-9567 page 3810	
A	WRIGHT J CLAIRE ET AL: "Immunization with the recombinant PorB outer membrane protein induces a bactericidal immune response against Neisseria meningitidis" INFECTION AND IMMUNITY, vol. 70, no. 8, August 2002 (2002-08), pages 4028-4034, XP002284892 ISSN: 0019-9567 page 4029	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	POLLARD A J ET AL: "The meningococcus tamed?" ARCHIVES OF DISEASE IN CHILDHOOD. ENGLAND JUL 2002, vol. 87, no. 1, July 2002 (2002-07), pages 13-17, XP002284893 ISSN: 1468-2044 page 15; table 2	
A	WO 01/09350 A (DALEMANS WILFRIED L J ;SMITHKLINE BEECHAM BIOLOG (BE); THIRY GEORG) 8 February 2001 (2001-02-08) examples 3-5	

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Information on patent family members

International Application No
PCT/IB 03/06281

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			PL	353891 A1	15-12-2003
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			ZA	200200824 A	22-09-2003